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09/856,944	07/16/2001	John Ernest Hart	GJE-68	6466
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SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION PO BOX 142950 GAINESVILLE, FL 32614-2950			AFREMOVA, VERA	
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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/856,944
Filing Date: July 16, 2001
Appellant(s): HART, JOHN ERNEST

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed on 4/29/2005.

S. a. d

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(1) *Real Party in Interest*

A statement identifying the real party in interest is contained in the brief.

(2) *Related Appeals and Interferences*

There are no related appeals or interferences.

(3) *Status of Claims*

The statement of the status of the claims contained in the brief is correct.

(4) *Status of Amendments After Final*

No amendment after final has been filed.

(5) *Summary of Invention*

The summary of invention contained in the brief is correct.

(6) *Issues*

The appellant's statement of the issues in the brief is correct.

(7) *Grouping of Claims*

The claims stand or fall together.

(8) *Claims Appealed*

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) *Prior Art of Record*

4,734,398

diZerega

3-1988

(10) *Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims as set forth in a prior Office Action, mailed on 11/24/2005.

Claim Rejections - 35 USC § 102/103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-5, 8 and 11-13 remain rejected under 35 U.S.C. 102(b) as anticipated by US 4,734,398 or, in the alternative, under 35 U.S.C. 103(a) as obvious over US 4,734,398 (diZerega).

The claims are directed to an endogenous material or a composition that is obtained by collecting ovarian venous blood of a female mammal post-oestrus, preparing plasma from the ovarian venous blood and partially purifying the material from the plasma to obtain fractions with molecular weights in the ranges 10-30 kD and/or 10-20 kD. The claimed composition is inducible in a post-oestrus female mammal by clomiphene and the claimed composition has ability to reduce mass of body organs including non-gonadal organs. Some claims are further drawn to the protocol of purifying the material by centrifuging blood, using ion exchange chromatography to elute fractions with gradient of 0-0.3 M NaCl.

US 4,734,398 discloses a material having ability to reduce organ mass (col. 3, line 55-58 or col. 10, lines 47, 61-64), which is obtained from ovarian venous blood of human female patients including patients with regular menstrual cycles. Blood collection is done on days 12-14 after last menstrual period that is around ovulation period (col. 8, line 61). The material is obtained by a process comprising steps of collecting an ovarian venous blood of female mammal (col. 8, line 63-65), preparing plasma from the ovarian venous blood by centrifugation (col. 9, lines 8, 18-19), partially purifying the material from the plasma by dialyzing with 10 kD exclusion membrane (col. 9, line 26), by chromatography and by washing with 0.5 M NaCl

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solutions (col. 9, lines 8-31). The patent teaches obtaining fractions with molecular weights in the ranges within 1-30 kD and/or 10-20 kD such as 12-15 kD, 14-18 kD, 22-25 kD that have capability of reducing organ mass or ovarian weight (col. 4, lines 19-21 and lines 27-31, col. 11, lines 52-54).

Thus, the cited patent US 4,734,398 discloses endogenous material or composition that is identical to the presently claimed material since the cited material is derived from the same source such as ovarian venous blood of a mammal, it has identical molecular weight such as 10-20 kD and it is said to have the same effect such as organ mass reduction as required for the claimed material. Furthermore, the material of the cited patent is collected at about time of ovulation or after and, thus, the final collected material is considered to be the same material that would have been induced by clomiphene in post-oestrus (post-ovulation) mammal within the meaning of the instant claims since clomiphene is a generic ovulation-inducing agent. Or, the collected material is considered to be the same regardless effects of clomiphene because the collected material would contain at least some amounts of the intended material since it is collected at about time of ovulation or after as required by claims. Consequently, the claimed invention is anticipated by the teaching of the cited patent US 4,734,398.

The characteristics of the claimed compound and /or feature of the claimed invention such as being "inducible ... by clomiphene" do not appear to be critical and distinguishable feature of the claimed invention over the prior art since the prior art material is collected at about and after ovulation time in a mammal or in "mammal post-oestrus" (post-ovulation), and, thus, it is reasonably expected to be present at least in some amounts in the ovarian blood as collected by the prior art method. Moreover, the prior art collected material is characterized by the same

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structure such as same molecular weight and by the same biological function such as organ weight reduction and, thus, it is reasonably believed to contain those material(s) that would have been induced by chlomiphene and found in ovarian venous blood of mammals.

In the alternative, even if the claimed material and/or its fractions are not identical to the referenced material/fractions with regard to some unidentified characteristics as related to the protocol of purification including the use of a particular ion exchange chromatography columns or specific concentrations of NaCl, for example, the differences between that which is disclosed and that which is claimed are considered to be so slight that the referenced material and/or fractions are likely to inherently possess the same characteristics of the claimed material particularly in view of the same characteristics which they have been shown to share that are identical molecular weight, identical effects related to the weight reduction and identical source of isolation. Thus the claimed invention would have been obvious to those skilled in the art within the meaning of USC 103. Accordingly, the claimed invention as a whole was at least prima facie obvious, if not anticipated by US 4,734,398, especially in the absence of evidence to the contrary.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-6, 8 and 11-14 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,734,398.

Claims 1, 3-5, 8 and 11-13 as explained above. Claims 6 and 14 are further drawn to the use of a sheep as source of mammalian ovarian venous blood for making claimed material.

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US 4,734,398 is relied upon as explained above. The particular disclosure is related to human patients as source of mammalian ovarian venous blood for making materials of interest. The generic disclosure identifies the use of human and porcine mammals as source of ovarian venous blood for making materials of interest. Thus, the cited patent is lacking a specific disclosure related to a sheep as source of isolation. However, the cited patent teaches that the disclosed material/fraction(s) are proteins (col. 8, line 61 and col. 10, last line) and that the activity of this material/fraction(s) is interspecies and that it is both produced and effective for various mammals (col. 3, lines 29-30).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to obtain the claimed material/fractions from various mammals including mammals such as human and sheep with a reasonable expectation of success in obtaining material/fractions having same effects as related to organ mass reduction and as related to ovulation or clomiphene-induced ovulation within the meaning of the claims because activity of same or similar proteins is interspecies and the same/similar proteins and effects are produced in various mammals as taught and/or suggested by the cited patent. One of skill in the art would have been motivated to use various mammals including sheep as the source of therapeutically valuable materials for the expected benefits in maximizing amounts of the collected materials. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary. The claimed subject matter fails to patentably distinguish over the state art as represented by the cited prior art. Therefore, the claims are properly rejected under 35 USC 103.

(11) Response to Argument

Appellant's arguments have been fully considered and the contents of declarations by Dr. John Ernest Hart and by Professor Iain James Clarke filed on 9/10/2004 have been reviewed but they are not found persuasive as related to the presently claimed invention.

A. Argument A (appeal brief pages 3-11). Appellant argues that the appellants' claims have several specific limitations that are not met by the diZerega's reference such as

- 1) materials must be inducible post-oestrus by clomiphene (appeal brief pages 3-5);
- 2) the claimed material reduces mass of organs including non-gonadal organs in live adult mammal (appeal brief pages 5-9); and
- 3) the material is purified from venous ovarian blood collected from a mammal post-oestrus (appeal brief pages 9-11).

1. Appellant's argument that the material must be inducible post-oestrus by clomiphene is not convincing because the as-filed specification clearly describes that "this step is optional" (instant specification page 1, line 25) and that "depending on factors such as the age of sheep, clomiphene induction may be unnecessary" (instant specification page 4, lines 1-2). Thus, clomiphene induction (treatment of blood donor with clomiphene) is not an absolute requirement for the claimed material to be present and to be found in ovarian venous blood accordingly to the description in the as-filed specification. Therefore, the prior art material, that is collected from the same source such as ovarian venous blood of mammals having oestrus cycle, is reasonably expected to comprise at least some amounts of the claimed material particularly in view that the prior art material is characterized by the same chemical structure

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such as same molecular weight and by the same biological function such as organ weight reduction as required for the claimed material.

Clomiphene is a known generic drug for induction of ovulation. The purpose and the effects of administering clomiphene to the donor of ovarian venous blood prior to ovarian venous blood collection are not described in as-filed specification. In the generic disclosure this step is optional. In the particular example clomiphene is administered to sheep post-oestrus (after ovulation) and the claimed material is collected from this sheep. The control experiments were carried out by collecting similar molecular weight fractions from clomiphene-untreated ovariectomised sheep. The sheep blood fractions were administered to rats and the differences in relative organ weight of rats were found variable (see fig. 4 and 5, for example). The figures demonstrate that some rat organs had relative weight decrease and some rat organs had relative weight increase. Thus, the effects of clomiphene on biological function of ovarian venous blood fractions are uncertain as described in the specification. The effects of clomiphene are not pointed out in the as-filed specification. Moreover, the use of clomiphene is optional.

Appellant further argues that the claimed material has been found to be induced by clomiphene independent of ovulation because clomiphene cannot re-induce ovulation after ovulation has occurred in mammals having oestrus cycle or in mammals having reoccurring ovulation (appeal brief page 4). However, the limitation as argued is not within the scope of the instant claims and this is not supported by disclosure in the instant as-filed specification. The claims are drawn to the use of “post-oestrus” mammals and thus, the claim specific mammals have to have oestrus cycle and to ovulate. Therefore, this feature (“induced by clomiphene independent of ovulation”) as argued is not within the scope of the instant claims as written. In

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the instant specification the only exemplified disclosure demonstrates the use of mammals such as sheep that ovulate and have oestrus cycle (instant specification paragraph bridging pages 5 and 6) as a source of the claimed material. The purpose and effects of administering clomiphene to donor of ovarian venous blood prior to blood collection are not described in as-filed specification. Therefore, the feature as argued is not supported by disclosure in the instant as-filed specification.

The Declaration by Professor Iain James Clarke filed on 9/10/2004 and arguments based thereon were fully considered before and have been reviewed. However they are not persuasive because the contents of declaration are related to alternative sources of isolation of “micrin” (“micrin” is a given name for the material described in the instant application; page 11, line 21) including brain tissue as alternative source of “micrin”. But this fact is neither within the scope of the instant claims nor it is described in the as-filed specification. Therefore, even if the feature of the appellant’s invention as argued such as material that is directly induced by clomiphene and that is independent of ovulation might distinguish over the prior art of record, this feature/characteristic of the claimed material is not described in the as-filed specification. The appellant’s presently claimed material is poorly characterized in the instant as-filed specification and it is not materially and functionally different from the prior art material. An advantage not disclosed in application cannot be urged as basis for allowing claims. *In re Lundberg* 117 USPQ 190 (CCPA 1958).

2. With regard to the claimed limitation drawn to the ability of the claimed material to reduce the mass of body organs including non-gonadal organs in live adult mammal (appeal brief pages 5-9) appellant argues that the prior art demonstrates a decrease in the increase that

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would otherwise have occurred (appeal pages 5 and 6). Nevertheless, reduction of organ mass has been shown for the prior art material that is collected from the same source and has the same molecular weight as the claimed material. The cited reference clearly teaches a “decrease in ovarian weight” (for example: see col. 10, line 48) upon administration of ovarian venous blood-derived fractions with the same molecular weight as the claimed material. In the diZeraga’s patent the rats had increased ovarian weight as result of gonadotropin treatment and the gonadotropin effect was inhibited by administration of ovarian venous blood fractions. Thus, inhibition of gonadotropin effects resulted in reduction of ovarian organ weight. Therefore, the disclosure of the cited patent falls within the scope of the presently claimed invention.

Appellant also argues the ability of the claimed material to reduce the mass of body organs including non-gonadal organs. The prior art clearly demonstrates effects of blood fractions on the gonadal organs such as ovaries. Yet, by the virtue of the open language “including” the claimed invention is open to limitations drawn to both non-gonadal and gonadal body organs including ovaries. Thus, this argument is not found persuasive with respect to the instant claims. Moreover, the appellant’s material(s) as disclosed had various effects on various organs including both reduction and increase on both ovaries and other organs, for example: see figures 1-5.

Appellant also argues the ability of the claimed material to reduce the mass of body in live adult mammals. Yet, the age of animals including the age of recipients of materials and the donor of materials is not defined in the as-filed specification. The 3 weeks old rats of the prior art (column 9, line 50) are neither embryonic nor new-born and they had body organs developed enough to evaluate their weights as demonstrated for rat ovaries. Therefore, the argument drawn

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to the differences, if any, between immature and adult animals as argued are not considered convincing.

3. As related to the feature that the claimed material is purified from venous ovarian blood collected from a mammal post-oestrus (appeal brief pages 9-11) appellant appears to argue that the prior art material might not have been collected "post-oestrus" as the claimed material because blood collection for the prior art material was done on days 12-14 after onset of the last menstrual period of female patients (column 8, lines 65-68). First, this argument appears to be contradictory to the previous argument that the appellant's material is independent of ovulation. Further, diZerega's disclosure is silent about how long were the menstrual cycles of the ovarian venous blood donors. Nevertheless, the blood collection was done in the middle of cycles and, thus, it is reasonable believe that blood collection was done at or after ovulation time in the ovulatory mammals and, thus, "in a mammal post-oestrus" within the meaning of the claims. Furthermore, the prior art active fractions were found only in those donors that had regular menstrual cycles or in ovulatory donors (column 10, lines 58-64). The appellant's blood fractions are derived from ovulatory sheep (page 5, example 1). The blood fractions derived from ovariectomised sheep were used as control fractions (page 9, lines 24-27). Thus, the claims were given broadest reasonable interpretation and in the light of specification.

The Declaration by Dr. Hart filed on 9/10/2004 (dated 8/02/2004) and arguments based thereon were fully considered before and have been reviewed. However they are not persuasive because the statements of the declaration that the prior art "FRP" and the appellant's "micrin" are demonstrably separate entities are speculative and unsupported. At the core, the appellant's material is poorly characterized as based on the as-filed specification and the applicant's claimed

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material is not characterized differently and/or better than the cited prior art material. Moreover, advantages, if any, that are not disclosed in application cannot be urged as basis for allowing claims. *In re Lundberg* 117 USPQ 190 (CCPA 1958).

B. Argument B (appeal brief pages 11-13).

Appellant argues that nothing in the diZerega reference would lead the skilled artisan to the advantageous material claimed by appellant and that apart from the same molecular weight there is no relevant physical or functional similarities between the prior art FRP (diZerega's ovarian venous blood fractions) and the appellant's material ("micrin"). Yet, no other structural or physical characteristic besides the molecular weight is claimed or known as disclosed for the appellant's material. The prior art ovarian venous blood fractions with the same molecular weights were shown to reduce the organ mass weight within the meaning of the claims.

Arguments that the appellant's material termed "micrin" is found in anovulatory patients, in peripheral blood and/or at different time during the female reproductive cycle (see appeal brief page 12, par. 3) are directed to advantages that are not disclosed in the as-filed specification.

Therefore, arguments based on some unidentified and/or undisclosed characteristics do not provide sufficient grounds for the evidence to the contrary to the claim rejection under 35 U.S.C. 103(a) as obvious over US 4,734,398.

An advantage not disclosed in application cannot be urged as basis for allowing claims. *In re Lundberg* 117 USPQ 190 (CCPA 1958).

For the above reasons, it is believed that the rejections should be sustained.

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Respectfully submitted,

Vera Afremova
Examiner
AU 1651



**VERA AFREMOVA
PRIMARY EXAMINER**

July 7, 2005

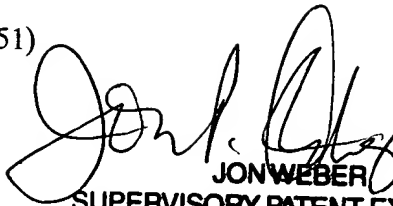
Conferees:

Michael G. Wityshyn (SPE AU 1651)



**Michael G. Wityshyn
Supervisory Patent Examiner
Technology Center 1600**

Jon P. Weber (SPE AU 1653)



**JON WEBER
SUPERVISORY PATENT EXAMINER**

SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950